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- a) contacting a yeast cell with the compound, which cell comprises (i) a first plasmid which expresses a fusion protein comprising a p66 subunit polypeptide of HIV-1 reverse transcriptase, (ii) a second plasmid which
5 expresses a fusion protein comprising a p51 subunit polypeptide of HIV-1 reverse transcriptase, and (iii) a reporter gene which is activated in the presence of a complex between the p66 subunit polypeptide and the p51 subunit polypeptide, and determining the level of
10 activity of the reporter gene in the cell in the presence of the compound; and
 - b) comparing the level of activity of the reporter gene determined in step (a) with a level of activity of the reporter gene determined in the absence of the
15 compound, wherein a decreased level of activity of the reporter gene in step (a) indicates that the compound inhibits formation of a complex between the p51 subunit polypeptide of HIV-1 reverse transcriptase and the p66 subunit polypeptide of HIV-1 reverse
20 transcriptase.
3. A method of determining whether a compound inhibits HIV-1 reverse transcriptase which comprises:
a) contacting a yeast cell with the compound, which cell
25 comprises (i) a first plasmid which expresses a fusion protein comprising a p66 subunit polypeptide of HIV-1 reverse transcriptase, (ii) a second plasmid which expresses a fusion protein comprising a p51 subunit polypeptide of HIV-1 reverse transcriptase, and (iii)
30 a reporter gene which is activated in the presence of

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- a complex between the p66 subunit polypeptide and the p51 subunit polypeptide, and determining the level of activity of the reporter gene in the cell in the presence of the compound; and
- 5 b) comparing the level of activity of the reporter gene determined in step (a) with a level of activity of the reporter gene determined in the absence of the compound, wherein an increased level of activity of the reporter gene determined in step (a) indicates
- 10 that the compound is an activator of the formation of the complex between the p51 subunit polypeptide of HIV-1 reverse transcriptase and the p66 subunit polypeptide of HIV-1 reverse transcriptase, thereby indicating that the compound inhibits HIV-1 reverse
- 15 transcriptase.
4. A method of determining whether a compound enhances formation of a complex between a p66 subunit polypeptide of HIV-1 reverse transcriptase and a p51
- 20 subunit polypeptide of HIV-1 reverse transcriptase which comprises:
- a) contacting a yeast cell with the compound, which cell comprises (i) a first plasmid which expresses a fusion protein comprising a p66 subunit polypeptide of HIV-1
- 25 reverse transcriptase, (ii) a second plasmid which expresses a fusion protein comprising a p51 subunit polypeptide of HIV-1 reverse transcriptase, and (iii) a reporter gene which is activated in the presence of a complex between the p66 subunit polypeptide and the
- 30 p51 subunit polypeptide, and determining the level of

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activity of the reporter gene in the cell in the presence of the compound; and

- b) comparing the level of activity of the reporter gene determined in step (a) with a level of activity of the reporter gene determined in the absence of the compound, wherein an increased level of activity of the reporter gene determined in step (a) indicates that the compound is an activator of the formation of the complex between the p51 subunit polypeptide of HIV-1 reverse transcriptase and the p66 subunit polypeptide of HIV-1 reverse transcriptase.
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5. A method of determining whether a compound inhibits HIV-1 reverse transcriptase which comprises:
- a) contacting a yeast cell with the compound, which cell comprises (i) a first plasmid which expresses a fusion protein comprising a first p66 subunit polypeptide of HIV-1 reverse transcriptase, (ii) a second plasmid which expresses a fusion protein comprising a second p66 subunit polypeptide of HIV-1 reverse transcriptase, and (iii) a reporter gene which is activated in the presence of a complex between the first p66 subunit polypeptide and the second p66 subunit polypeptide, and determining the level of activity of the reporter gene in the cell in the presence of the compound; and
- b) comparing the level of activity of the reporter gene determined in step (a) with a level of activity of the reporter gene determined in the absence of the compound, wherein a decreased level of activity of the

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subunit polypeptide of HIV-1 reverse transcriptase and the second p66 subunit polypeptide of HIV-1 reverse transcriptase.

- 5 7. A method of determining whether a compound inhibits HIV-1 reverse transcriptase which comprises:
 - a) contacting a yeast cell with the compound, which cell comprises (i) a first plasmid which expresses a fusion protein comprising a first p66 subunit polypeptide of HIV-1 reverse transcriptase, (ii) a second plasmid which expresses a fusion protein comprising a second p66 subunit polypeptide of HIV-1 reverse transcriptase, and (iii) a reporter gene which is activated in the presence of a complex between the first p66 subunit polypeptide and the second p66 subunit polypeptide, and determining the level of activity of the reporter gene in the cell in the presence of the compound; and
 - b) comparing the level of activity of the reporter gene determined in step (a) with a level of activity of the reporter gene determined in the absence of the compound, wherein an increased level of activity of the reporter gene in step (a) indicates that the compound is an activator of the formation of the complex between the first p66 subunit polypeptide of HIV-1 reverse transcriptase and the second p66 subunit polypeptide of HIV-1 reverse transcriptase, thereby indicating that the compound inhibits HIV-1 reverse transcriptase.

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domain.

17. The method of any one of claims 1-8, wherein (a) the fusion protein expressed by the first plasmid comprises a peptide having a transcription activation domain, and (b) the fusion protein expressed by the second plasmid comprises a peptide having a DNA binding domain.
18. The method of claim 17, wherein the DNA binding domain is a LexA DNA binding domain.
19. The method of claim 18, wherein the peptide having a DNA binding domain comprises LexA amino acid residues 1-87.
20. The method of claim 18, wherein the peptide having a DNA binding domain comprises LexA amino acid residues 1-202.
21. The method of claim 17, wherein the DNA binding domain is a GAL4 DNA binding domain.
22. The method of claim 17, wherein the transcription activation domain is a GAL4 transcription activation domain.
23. The method of claim 22, wherein the transcription activation domain comprises GAL4 amino acid residues 768-881.

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epitope tag, and a peptide comprising six consecutive
alanine residues, wherein the Gal4 peptide is bound at
its C-terminal amino acid to the N-terminal amino acid
of the influenza hemagglutinin (HA) epitope tag,
5 wherein the influenza hemagglutinin (HA) epitope tag
is bound at its C-terminal amino acid to the N-
terminal amino acid of the peptide comprising six
consecutive alanine residues, wherein the peptide
comprising six consecutive alanine residues is bound
10 at its C-terminal amino acid to the N-terminal amino
acid of the p66 subunit polypeptide; and (b) the
fusion protein expressed by second plasmid comprises
a peptide comprising a LexA protein DNA binding
domain, wherein the p51 subunit polypeptide is bound
15 at its C-terminal amino acid to the N-terminal amino
acid of the peptide comprising a LexA protein DNA
binding domain.

36. The method of any one of claims 1-4, wherein (a) the
20 fusion protein expressed by the first plasmid
comprises a Gal4 peptide corresponding to amino acids
768-881 of Gal4, an influenza hemagglutinin (HA)
epitope tag, and a peptide comprising six consecutive
alanine residues, wherein the Gal4 peptide is bound at
25 its C-terminal amino acid to the N-terminal amino acid
of the influenza hemagglutinin (HA) epitope tag,
wherein the influenza hemagglutinin (HA) epitope tag
is bound at its C-terminal amino acid to the N-
terminal amino acid of the peptide comprising six
30 consecutive alanine residues, wherein the peptide

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comprising six consecutive alanine residues is bound at its C-terminal amino acid to the N-terminal amino acid of the p66 subunit polypeptide; and (b) the fusion protein expressed by second plasmid comprises a peptide comprising a LexA protein DNA binding domain, wherein peptide comprising a LexA protein DNA binding domain is bound at its C-terminal amino acid to the N-terminal amino acid of the p51 subunit polypeptide.

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37. The method of any one of claims 1-4, wherein (a) the fusion protein expressed by the first plasmid comprises a Gal4 peptide corresponding to amino acids 768-881 of Gal4, an influenza hemagglutinin (HA) epitope tag, and a peptide comprising six consecutive alanine residues, wherein the Gal4 peptide is bound at its C-terminal amino acid to the N-terminal amino acid of the influenza hemagglutinin (HA) epitope tag, wherein the influenza hemagglutinin (HA) epitope tag is bound at its C-terminal amino acid to the N-terminal amino acid of the peptide comprising six consecutive alanine residues, wherein the peptide comprising six consecutive alanine residues is bound at its C-terminal amino acid to the N-terminal amino acid of the p66 subunit polypeptide; and (b) the fusion protein expressed by second plasmid comprises a peptide comprising a Gal4 protein DNA binding domain, which peptide comprising a Gal4 protein DNA binding domain is bound at its C-terminal amino acid to the N-terminal amino acid of the p51 subunit

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polypeptide.

38. The method of any one of claims 1-4, wherein (a) the fusion protein expressed by the first plasmid comprises a Gal4 peptide corresponding to amino acids 768-881 of Gal4, wherein the Gal4 peptide is bound at its C-terminal amino acid to the N-terminal amino acid of the p66 subunit polypeptide; and (b) the fusion protein expressed by second plasmid comprises a peptide comprising a LexA protein DNA binding domain, wherein the p51 subunit polypeptide is bound at its C-terminal amino acid to the N-terminal amino acid of the peptide comprising a LexA protein DNA binding domain.
39. The method of any one of claims 1-4, wherein (a) the fusion protein expressed by the first plasmid comprises a Gal4 peptide corresponding to amino acids 768-881 of Gal4, wherein the Gal4 peptide is bound at its C-terminal amino acid to the N-terminal amino acid of the p66 subunit polypeptide; and (b) the fusion protein expressed by second plasmid comprises a peptide comprising a LexA protein DNA binding domain, which peptide comprising a LexA protein DNA binding domain is bound at its C-terminal amino acid to the N-terminal amino acid of the p51 subunit polypeptide.
40. The method of any one of claims 1-4, wherein (a) the fusion protein expressed by the first plasmid comprises a Gal4 peptide corresponding to amino acids

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768-881 of Gal4, wherein the Gal4 peptide is bound at its C-terminal amino acid to the N-terminal amino acid of the p66 subunit polypeptide; and (b) the fusion protein expressed by second plasmid comprises a peptide comprising a Gal4 protein DNA binding domain, which peptide comprising a Gal4 protein DNA binding domain is bound at its C-terminal amino acid to the N-terminal amino acid of the p51 subunit polypeptide.

- 5 41. The method of any one of claims 5-8, wherein (a) the fusion protein expressed by the first plasmid comprises a peptide comprising a LexA protein DNA binding domain, wherein the p66 subunit polypeptide is bound at its C-terminal amino acid to the N-terminal amino acid of the peptide comprising a LexA protein DNA binding domain; and (b) the fusion protein expressed by the second plasmid comprises a Gal4 peptide corresponding to amino acids 768-881 of Gal4, an influenza hemagglutinin (HA) epitope tag, and a peptide comprising six consecutive alanine residues, wherein the Gal4 peptide is bound at its C-terminal amino acid to the N-terminal amino acid of the influenza hemagglutinin (HA) epitope tag, wherein the influenza hemagglutinin (HA) epitope tag is bound at its C-terminal amino acid to the N-terminal amino acid of the peptide comprising six consecutive alanine residues, wherein the peptide comprising six consecutive alanine residues is bound at its C-terminal amino acid to the N-terminal amino acid of the p66 subunit polypeptide.

42. A method of making a pharmaceutical composition which comprises:
 - a) determining whether a compound inhibits HIV-1 reverse transcriptase by the method of any one of claims 1-8;
 - b) recovering the compound if it is determined to inhibit HIV-1 reverse transcriptase; and
 - c) admixing the compound with a pharmaceutically acceptable carrier.
43. A method of inhibiting formation of a complex between the p51 subunit polypeptide of HIV-1 reverse transcriptase and a p66 subunit polypeptide of HIV-1 reverse transcriptase, which comprises contacting either (1) the p51 subunit polypeptide, (2) the p66 subunit polypeptide, or (3) both the p51 subunit polypeptide and the p66 subunit polypeptide, with an effective amount of a compound determined to do so by the method of claim 2, so to thereby inhibit formation of a complex between the p51 subunit polypeptide of HIV-1 reverse transcriptase and a p66 subunit polypeptide of HIV-1 reverse transcriptase.
44. A method of enhancing formation of a complex between the p51 subunit polypeptide of HIV-1 reverse transcriptase and a p66 subunit polypeptide of HIV-1 reverse transcriptase, which comprises contacting either (1) the p51 subunit polypeptide, (2) the p66 subunit polypeptide, or (3) both the p51 subunit polypeptide and the p66 subunit polypeptide, with an

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effective amount of a compound determined to do so by
the method of claim 4, so to thereby enhance formation
of a complex between the p51 subunit polypeptide of
HIV-1 reverse transcriptase and a p66 subunit
5 polypeptide of HIV-1 reverse transcriptase.

45. A method of inhibiting formation of a complex between
a first p66 subunit polypeptide of HIV-1 reverse
transcriptase and a second p66 subunit polypeptide of
10 HIV-1 reverse transcriptase, which comprises
contacting either (1) the first p66 subunit
polypeptide, (2) the second p66 subunit polypeptide,
or (3) both the first p66 subunit polypeptide and the
second p66 subunit polypeptide, with an effective
15 amount of a compound determined to do so by the method
of claim 6, so to thereby inhibit formation of a
complex between the first p66 subunit polypeptide of
HIV-1 reverse transcriptase and the second p66 subunit
polypeptide of HIV-1 reverse transcriptase.

20 46. A method of enhancing formation of a complex between
a first p66 subunit polypeptide of HIV-1 reverse
transcriptase and a second p66 subunit polypeptide of
HIV-1 reverse transcriptase, which comprises
25 contacting either (1) the first p66 subunit
polypeptide, (2) the second p66 subunit polypeptide,
or (3) both the first p66 subunit polypeptide and the
second p66 subunit polypeptide, with an effective
amount of a compound determined to do so by the method
30 of claim 8, so to thereby enhance formation of a

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complex between the first p66 subunit polypeptide of HIV-1 reverse transcriptase and the second p66 subunit polypeptide of HIV-1 reverse transcriptase.

- 5 47. The method of any one of claims 43-46, wherein the HIV-1 reverse transcriptase is present in a subject and the contacting is effected by administering the compound to the subject.
- 10 48. The method of claim 47, wherein the compound is administered orally, intravenously, subcutaneously, intramuscularly, topically or by liposome-mediated delivery.
- 15 49. The method of claim 47, wherein the subject is a human being, a primate, an equine, an opine, an avian, a bovine, a porcine, a canine, a feline or a mouse.
- 20 50. The method of claim 47, wherein the effective amount of the compound is between about 1mg and about 50mg per kg body weight of the subject.
- 25 51. The method of claim 50, wherein the effective amount of the compound is between about 2mg and about 40mg per kg body weight of the subject.
- 30 52. The method of claim 51, wherein the effective amount of the compound is between about 3mg and about 30mg per kg body weight of the subject.

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53. The method of claim 52, wherein the effective amount of the compound is between about 4mg and about 20mg per kg body weight of the subject.
- 5 54. The method of claim 53, wherein the effective amount of the compound is between about 5mg and about 10mg per kg body weight of the subject.
55. The method of claim 54, wherein the compound is
10 administered at least once per day.
56. The method of claim 47, wherein the compound is administered daily.
- 15 57. The method of claim 47, wherein the compound is administered every other day.
58. The method of claim 47, wherein the compound is administered every 6 to 8 days.
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59. The method of claim 47, wherein the compound is administered weekly.
60. A compound determined to be capable of inhibiting
25 formation of a complex between a p51 subunit polypeptide of HIV-1 reverse transcriptase and a p66 subunit polypeptide of HIV-1 reverse transcriptase by the method of claim 2.
- 30 61. A compound determined to be capable of enhancing

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formation of a complex between a p51 subunit polypeptide of HIV-1 reverse transcriptase and a p66 subunit polypeptide of HIV-1 reverse transcriptase by the method of claim 4.

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62. A compound determined to be capable of inhibiting formation of a complex between a first p66 subunit polypeptide of HIV-1 reverse transcriptase and a second p66 subunit polypeptide of HIV-1 reverse transcriptase by the method of claim 6.

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63. A compound determined to be capable of enhancing formation of a complex between a first p66 subunit polypeptide of HIV-1 reverse transcriptase and a second p66 subunit polypeptide of HIV-1 reverse transcriptase by the method of claim 8.

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64. A composition which comprises the compound of any one of claims 60-63 and a carrier.

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